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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/499,526

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Kuanghui Lu

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EXAMINER

DEBERRY, REGINA M

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/499,526	LU ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 December 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/05</u> . | 6) <input type="checkbox"/> Other: _____ |

Status of Application, Amendments and/or Claims

The amendment filed 17 December 2004 has been entered in full. Claims 1-12, 14, 22, 24, 34, 38, 40-44, 47-49, 51, 63, 64, 68, 72, 95 and 99 are cancelled. New claims 120-123 were added. Claims 25-27, 35-37, 52, 55, 56, 61, 62, 65-67, 69-71, 73-75, 79-84, 86 and 113-115 are withdrawn from consideration as being drawn to a non-elected group. It is noted that claim 61 was inadvertently missed from being withdrawn from consideration, as it is depends from a claim drawn to a non-elected group.

Claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, 116-123 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement (IDS) filed 03 January 2005 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Withdrawn Objections And/Or Rejections

The objection to claims 13, 90, 92 and 93 as set forth at page 8 of the previous Office Action (15 June 2004) is *withdrawn* in view of Applicant's arguments (17 December 2004).

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 109, 112, and 119 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pages 3-8 of the previous Office Action (15 June 2004).

Applicant reiterates the Examiner's rejection from the previous Office Action. Applicant states that the second ground for rejection is that the specification allegedly fails to enable claims directed to methods of treating a disease in animal, as it is alleged that the physiological response of cells in culture does not necessarily or predictably correlate with an effect *in vivo*. Applicant argues that a similar rejection was raised by the Patent Office on page 8 of the March 12, 2001 and page 10 of the August 27, 2001 Office Actions. Applicant maintains that these rejections were overcome by Applicants' response filed January 28, 2002 and that a copy of the appropriate pages and exhibits of the response are attached. Applicant argues that ample evidence is provided of *in vitro* functions of PYY showing a strong correlation to *in vivo* results. Applicant submits that these data are sufficient for one of ordinary skill in the art to reasonably believe that the PYY results *in vitro* would be predictive of results *in vivo*. Applicant states that provided are *in vivo* data of PYY's ability to control glucose levels in rats predisposed to diabetes.

Applicant's arguments have been fully considered but not deemed persuasive for the following reasons. The instant claims are drawn to a method of treating a disease associated with altered glucose metabolism, wherein the disease is hyperlipidemia or hyperlipoproteinemia. Exhibit C presented by Applicant demonstrates the effects of PYY in a Zucker Diabetic Fatty rat. PYY regulated the glucose level. The results from the Zucker Diabetic rat could correlate with treating diseases/conditions such as insulin resistance, glucose intolerance, glucose non-responsiveness or Type II diabetes mellitus, however, the results from Exhibit C are not applicable to treating hyperlipidemia or hyperlipoproteinemia. The On-Line Medical dictionary teaches the definition of hyperlipidemia or hyperlipoproteinemia as elevated concentrations of any or all of the lipids in the plasma, such as cholesterol, triglycerides and lipoproteins (please see reference). Thus, while PYY may be treating altered glucose metabolism in an animal suffering from hyperlipidemia or hyperlipoproteinemia, the results from Exhibit C do not demonstrate PYY actually **treating** hyperlipidemia or hyperlipoproteinemia.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claims 13, 21, 23, 33, 45, 87, 88, 89, 90, 91, 92, 93, 94 and 102 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

the instant methods wherein a PYY agonist or biologically active fragment thereof has the following functions of PYY (a) binds a PYY receptor **and** (b) promotes glucose-

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responsiveness of pancreatic islets or pancreatic cells **and optionally** (c) inhibits intestinal motility or (d) inhibits mesenteric blood flow; or (e) mediates gastric, pancreatic, or intestinal exocrine secretion; or (f) stimulates net absorption of nutrients, does not reasonably provide enablement for:

the instant methods wherein a PYY agonist or biologically active fragment thereof **has one** or more of the following functions of PYY.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The scope of patent protection sought by Applicant as defined by the claims fails to bear a reasonable correlation with the scope of enabling disclosure set forth in the specification because the instant claims read on the PYY agonist or biologically active fragment thereof having **only one of the recited functions of PYY**. Thus, the PYY agonist or biologically active fragment can just have the function of binding a PYY receptor (a) or just stimulating net absorption of nutrients (f) or just inhibiting mesenteric blood flow (d). The instant methods are drawn to inducing or enhancing the glucose-responsiveness of impaired pancreatic islets or pancreatic cells, inducing or enhancing glucose metabolism in an animal having a disease associated with abnormal glucose metabolism and maintaining or restoring normal pancreatic islet function to impaired glucose responsive or sensing islets or cells. To be fully enabled, the PYY agonist or biologically active fragment thereof **must** have the PYY functions of binding a PYY receptor **and** promoting glucose-responsiveness of pancreatic islets or pancreatic cells.

Due to the large quantity of experimentation necessary to induce/enhance glucose-responsiveness of impaired pancreatic islets and pancreatic cells, induce/enhance glucose metabolism in an animal and maintain/restore normal pancreatic islet function with a PYY agonist or biologically active fragment thereof that does not bind a PYY receptor and that does not promote glucose-responsiveness of pancreatic islets or pancreatic cells, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention and the breadth of the claims which fail to fully recite the functional limitations of PYY agonist or biologically active fragment thereof necessary to enable the instant claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 21, 23, 33, 45, 87, 92, 93 and 122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13, 45, 87 and 92 are indefinite because of the recitation, "...pancreatic islet or cell...". It is not clear what type of cell is being claimed. It is suggested that the instant claims be amended to recite "**pancreatic cell**".

Claims 13, 21, 23, 33, 45 and 93 are indefinite because of the recitation,

".....an amino acid sequence having a **corresponding** nucleic acid sequence...". The instant claims read on an amino acid/nucleic acid complex. It is suggested that the instant claims be amended to recite, "an amino acid sequence **encoded by** a nucleic acid sequence".

Claim 122 is drawn to a PYY agonist or fragment PYY wherein the PYY agonist or fragment is PYY(3-36). A claim is indefinite in the recitation of amino acid positions (or nucleotide sequences) in the absence of a referenced SEQ ID NO:.. It is not known whether PYY(3-36) recited in the instant claim corresponds to the same PYY comprising SEQ ID NO:3. The metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless—

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23, 89, 102-105, 108, 111 and 118 are rejected under 35 U.S.C. 102(b) as being anticipated by Morley *et al.*, Life Sciences, Vol. 41, pg 2157-2165 (1987).

The instant claims are drawn to a method for treating a disease associated with altered glucose metabolism, comprising administering to an animal having a disease associated with altered glucose metabolism, an amount of a composition comprising PYY (or PYY agonist or biologically fragment thereof) wherein said disease is obesity.

Morley *et al.* teach the administration of PYY to mice (page 2158, last paragraph). Morley *et al.* teach that the peripheral administration of peptide YY (PYY) caused weight loss (abstract; page 2158 last paragraph and Table 5). Morley *et al.* state that neurotransmitters that enhance feeding centrally cause weight loss when given peripherally. Morley *et al.* state that this is best demonstrated in this study where PYY caused weight loss. Morley *et al.* teach that PYY have been shown to produce weight gain after central administration, yet peripherally, PYY caused weight loss, without altering food intake (page 2163, last paragraph-page 2164, first paragraph).

The polynucleotide sequence of PYY is SEQ ID NO:1 and the polypeptide sequence of PYY is SEQ ID NO:3. Thus the PYY of Morley *et al.* would comprise an amino acid sequence having a corresponding nucleic acid sequence wherein the nucleic acid hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65C, to SEQ ID NO: 1 (applies to claims 23 and 102-105). The PYY of Morley *et al.* would have the following functions of PYY (a) binds a PYY receptor and (b) promotes glucose-responsiveness of pancreatic islets or pancreatic cells;(c) inhibits intestinal motility;(d) inhibits mesenteric blood flow;(e) mediates gastric, pancreatic, or intestinal exocrine secretion; or (f) stimulates net absorption of nutrients (**applies to claims 23, 89, 102-105**). A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Lastly, obesity is a disease that can be associated with altered glucose metabolism (**applies to claims 108, 111 and 118**).

Conclusion
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RMD
3/16/05



ELIZABETH C. KEMMERER
PATENT EXAMINER

Continuation of Disposition of Claims: Claims pending in the application are 13,15-21,23,25-33,35-37,39,45,46,50,52-62,65-67,69-71,73-94,96-98 and 100-123.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 25-27,35-37,52,55,56,61,62,65-67,69-71,73-75,79-84,86 and 113-115.

Continuation of Disposition of Claims: Claims rejected are 13,15-21,23,28-33,39,45,46,50,53,54,57-60,76-78,85,87-94,96-98,100-112 and 116-123.